NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES

The National Institute of Arthritis and Metabolic Diseases (NIAMD) is one of the National Institutes of Health (NIH) at Bethesda, Md., a suburb of Washington, D. C. NIH is the principal medical research center of the U. S. Department of Health, Education, and Welfare.

FOREWORD

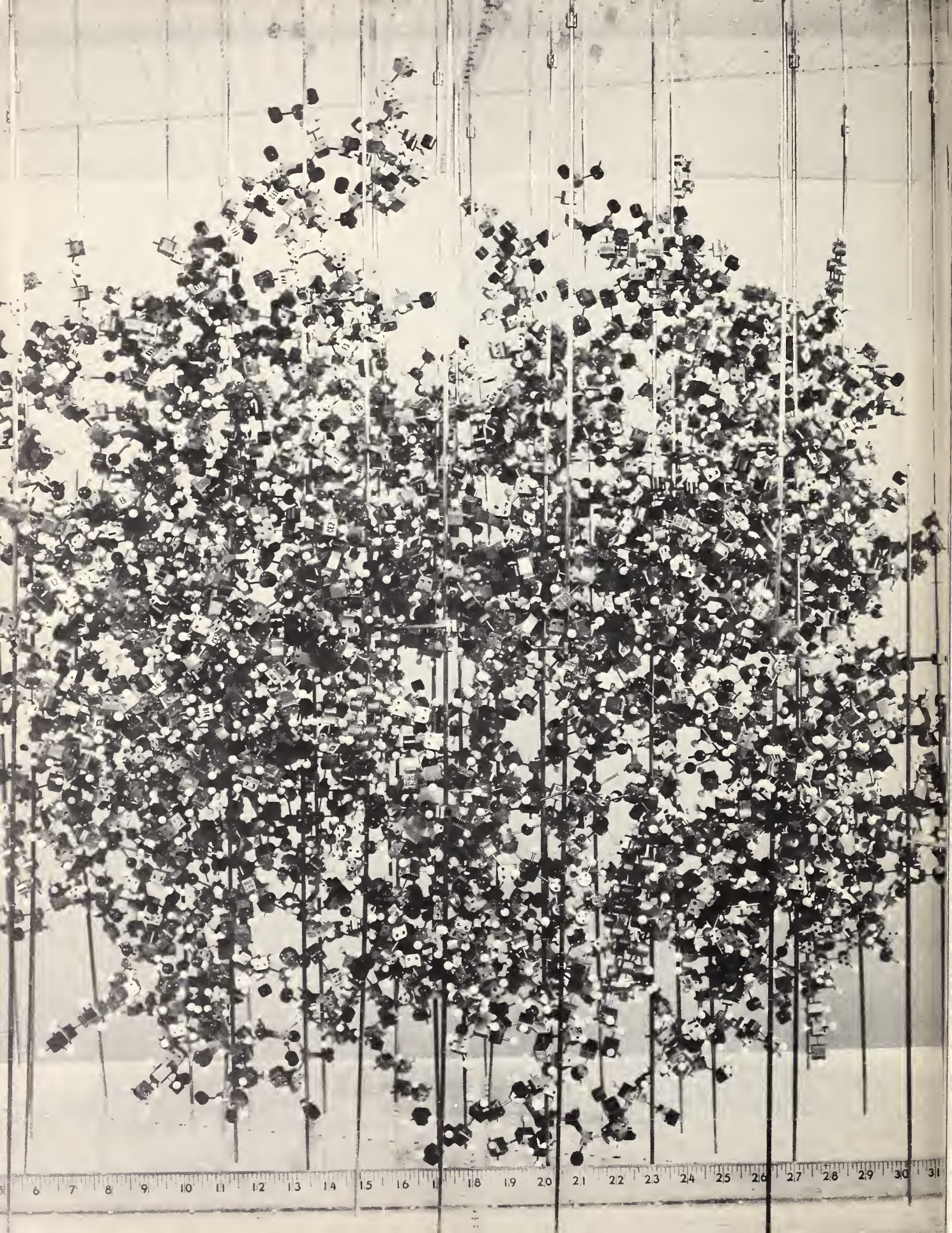
Of all the afflictions plaguing man through the ages, none have caused more misery than the chronic diseases that are the concern of the National Institute of Arthritis and Metabolic Diseases (NIAMD). These persistent, recurring disorders are seldom fatal, but rather torment their victims over prolonged periods. Much too often, the arthritic and metabolic disorders are neglected until they cause serious disability.

Modern medical science has demonstrated clearly that basic studies of the nature and modes of action of these diseases offer the greatest hope of wiping them from the face of the earth, or, at least, minimizing their ravages to the point where they are no longer a major threat to public health. Thus, the NIAMD has an important stake in conducting and supporting research in fundamental sciences, such as biochemistry, enzymology, molecular biology, histology, pathology, pharmacology, toxicology, and genetics, where these disciplines are pertinent to the Institute's sphere of interest.

This sphere is wide, encompassing a great number and diversity of illnesses. Arthritis, itself, comprises a group of disorders characterized by inflammation and impairment of the joints. The so-called metabolic diseases, characterized by a specific fixed disorder in body chemistry, constitute a huge variety of illnesses, ranging from diabetes, which affects about 4 million Americans, to comparatively rare conditions such as maple syrup urine disease. In addition, for years NIAMD has accepted an even broader challenge, bringing its resources to bear in other major research areas. Diseases of the digestive system, such as peptic ulcer and ulcerative colitis; liver diseases; disorders of blood, bone, and kidney; urology; orthopedic surgery; skin diseases, such as psoriasis; endocrine disorders; and nutrition are other major areas of responsibility of the Institute.

We hope that this brochure will reflect the scope, the essential excitement, and the very great promise of basic and clinical investigations of the National Institute of Arthritis and Metabolic Diseases.

G. Donald Whedon, M.D.
Director
National Institute of Arthritis
and Metabolic Diseases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HISTORY

The National Institute of Arthritis and Metabolic Diseases (NIAMD), one of the National Institutes of Health (NIH) at Bethesda, Md., was established by the 81st Congress through Public Law 692 enacted August 15, 1950. At that time, NIAMD acquired the laboratories of the Experimental Biology and Medicine Institute, (EBMI) which had been a "general" Division of NIH. Through these laboratories, NIAMD can trace its origins back some 80 years. Its tradition of nutrition research, for example, stems from the classic work on pellagra as a vitamin deficiency disease by Dr. Joseph Goldberger (assigned to this problem by the Public Health Service in 1914) and by his student, Dr. W. H. Sebrell, who later served as Director of the EBMI, as the first Director of NIAMD, and, subsequently, as Director of the NIH until 1955.

The first operating funds of NIAMD in Fiscal year 1951 amounted to about $2,400,000. With the growth of Institute programs, recent yearly budgets appropriated to the Institute by the Congress have totalled over $140,000,000 for research at Bethesda, for extramural grant-supported investigations and contract work, and for fellowship and training support.

Over the years, NIAMD, originally created for the study of arthritic disorders and diverse diseases of metabolism, has expanded its program, with direct Congressional mandate to move forward energetically in specific areas, as, for example, in the development of more efficient and less expensive artificial kidney machines. Today it is the principal Federal agency conducting and supporting research against the broad array of diseases that are its responsibility.

The years during which this Institute has developed have been those during which basic research has come of age. Fundamental studies in the life sciences once regarded as esoteric now are recognized as prelude to vital public health measures. With its evolution from laboratories noted for their pioneering work in experimental medicine and biology, NIAMD has become a center for new knowledge of genetics and metabolism, as well as for disease-oriented studies of arthritis, diabetes, cystic fibrosis, gastrointestinal disorders, and many others. Thus, the Institute's sphere of interest will remain broad and its influence will continue to be a significant factor in the Nation's health advances.

This 3-dimensional model of the hemoglobin molecule, magnified about 127 million times, is foot-locker size. Built by an NIAMD scientist, it helps to clarify the molecular mechanisms involved in sickle cell anemia. This hereditary disorder, striking Negroes almost exclusively, is the result of abnormal hemoglobin—the oxygen-carrying element in red blood cells. Affected cells "sickle"—lose their customary shape, take on a half-moon appearance, and block circulation by clogging small blood vessels. No way has yet been discovered to counter the oxygen deficiency but case-finding and treatment have improved in recent years.

The major portion of funds appropriated by Congress for the Institute's activities is used to provide grants to non-Federal scientists at medical centers and universities across the country. This money supports both laboratory and clinical research and makes possible the training of many research scientists. Here Institute staff members process some of the many grant applications for research support.

A limited number of patients, who have been referred by their physicians, participate in studies of arthritis and other conditions at the NIH Clinical Center research hospital.

THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES (NIAMD)

THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES (NIAMD) bears responsibility for complex and disabling diseases that rank first in prevalence in the United States. An attitude of hopelessness formerly prevailed about them, but today the question is no longer *whether* these disorders can be controlled but rather *when?* Moreover, many of these diseases are already amenable to effective measures or treatment as a result of research.

Physicians, biochemists, mathematicians, microbiologists, geneticists, and pharmacologists—scientists of scores of disciplines—and supporting workers from glass-washers to secretaries work together at Institute laboratories and clinics in Bethesda and in epidemiological and field studies throughout the world. Through its largest effort, the extramural grants program, the NIAMD supports many hundreds of research and training projects in non-federal institutions in every region of the Nation.

This is the hand of a person suffering from gout, before use of hypouricemic drugs brought marked improvement by preventing or reducing the accumulation of urate crystals that cause the lumps on fingers and knuckles seen in this photograph. Other drugs are used to control the acute pain, once the almost inevitable consequence of gout.

ARTHRITIS AND RHEUMATIC DISEASES

Over 13 million Americans suffer from arthritis, a group of diseases characterized by inflammation and impairment of the joints. While seldom fatal in itself, arthritis has the unenviable distinction of being the foremost crippler in the United States, bringing widespread pain and privation. The cost to the Nation is estimated at $2 billion yearly.

Of the many forms of rheumatic disease, rheumatoid arthritis is the most serious and crippling. It is a systemic disease which affects not only the joints, but many other organs and tissues in the body. Rheumatoid arthritis attacks all age groups, including children, striking three females to every male. The majority of its victims are not elderly persons (as in osteoarthritis, which is more common but less disabling) but are young and middle-aged adults in their most productive years.

The primary cause of rheumatoid arthritis continues to elude relentless pursuit. There are two leading theories, supported by impressive evidence. One holds that rheumatoid arthritis is the result of autoimmunity, in which the body produces abnormal antibodies directed against some of its own tissue components. The other theory holds that the disorder (which may well be based on a mechanism of abnormal immune reactions) may be induced originally by an infectious process. Mycoplasma—microorganisms with characteristics somewhere between bacteria and viruses—or viruses of the genus *Bedsonia* are currently implicated as the most likely agents.

These two theories, which are not conflicting as one factor can lead to the other, will continue to be investigated intensively in numerous research projects. In addition, emphasis will be placed on studies of cartilage and joint mechanics and lubrication processes.

While there is as yet no cure for rheumatoid arthritis, modern medicine is developing effective drugs to allay its pain and sophisticated surgical and rehabilitative techniques to prevent or correct joint damage. With early diagnosis and proper treatment, 9 out of 10 patients are benefited, and 7 out of 10 avoid severe disablement.

VICTORY OVER GOUT

Many researchers who believe that rheumatoid arthritis may soon be successfully treated point to gout as an example of an inflammatory joint disorder that has harassed man throughout history but which now can be controlled.

Once considered the result of overindulgence in food and drink, gout is now understood to be caused by basic defects in body chemistry. Recently, through work by NIAMD scientists and other researchers, these basic metabolic defects—increased production of uric acid (a normal constituent of the blood and urine) and/or impaired uric acid urinary excretion—have been explained, as has the mechanism of the highly painful attacks of gouty arthritis.

Today, through drugs that regulate uric acid levels in patients and overcome pain and joint damage, gout can be an agony of the past. Here we have a perfect example of an arthritic and metabolic disease that responds to up-to-date treatment and can be well controlled if diagnosed and treated promptly. Basic research has provided knowledge that now affords a comfortable, normal existence to the patient.

GENETIC DISEASES OF METABOLISM

In view of the fact that metabolism is the term given to the sum total of the thousands of chemical reactions that take place in each cell of the body, it is easy to see how great the chances are for a "metabolic error" which is reflected in disease, and how wide a field the phrase "metabolic research" encompasses.

THE GENETIC CODE

It has long been known that we look and act like our parents, whether we're anteaters or Eskimos, because hereditary traits are passed down from one generation to the next in the genes. Only recently, however, through the initial cracking of the so-called "genetic code" by NIAMD investigators and others has the mechanism of this replication process been revealed.

The genetic code, to which all animals and plants owe their existence as separate and distinct species, is a system of messages assembled and transmitted by deoxyribonucleic acid (DNA). This is the substance in cells that embodies the genetic information which guides the making of a new living organism that resembles its parent. These messages consist of a set of instructions put down in a chemical formula. The precise nature and sequence of the chemical substances determine what the progeny cell will be and how it will function.

The significance of DNA, which has been called the "blueprint" molecule cannot be overstated. It may hold the answers to what goes wrong in a cancerous cell, and how to control hereditary diseases. Major research efforts are continuing in this exciting and promising area.

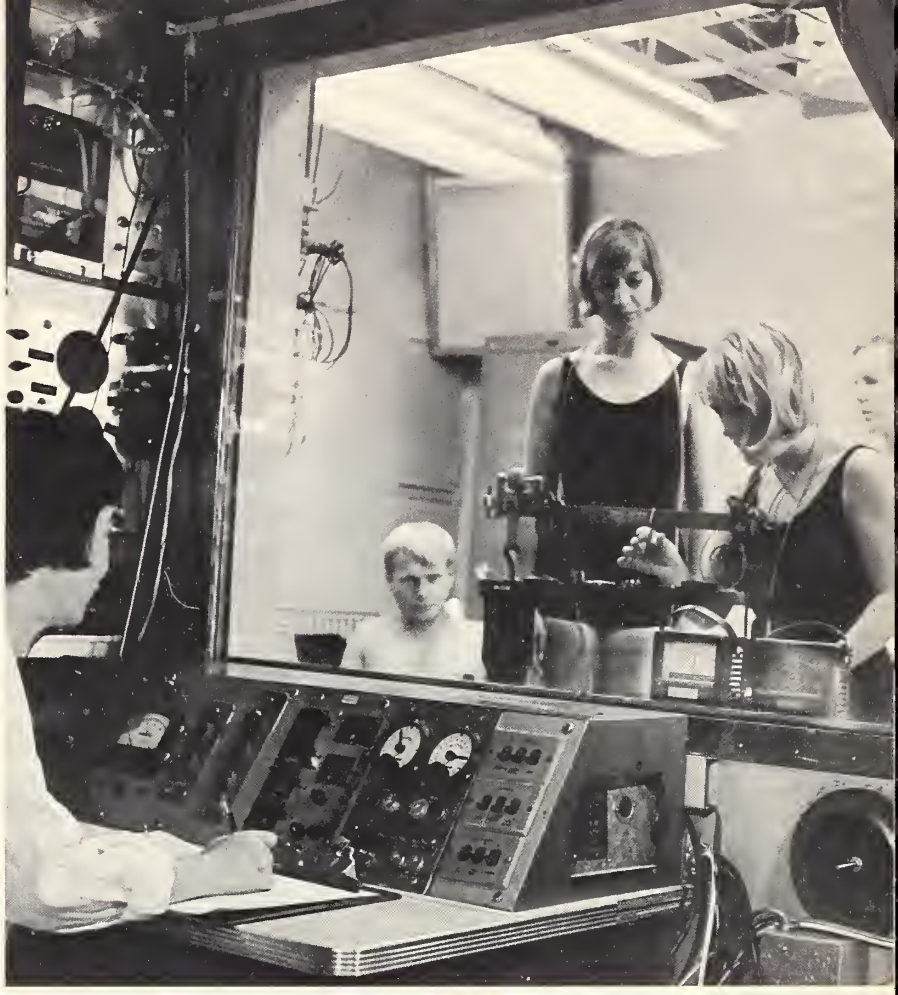
INBORN ERRORS OF METABOLISM

Long before the intricate biochemical principles of genetics were unraveled, it was known that metabolic "errors"—defects in the chemistry of cellular processes—can cause disease.

Living tissue is composed primarily of proteins which are the foundation of form and function. Malfunction can result from even a single error in the metabolic instructions, in the exquisitely sophisticated "data processing" of the genetic code. Failure to include or properly position one specific amino acid, for example, can block the normal completion of basic chemical reactions essential to healthy cells.

Sometimes the error is minor and results in nothing more troublesome than a lack of coloration, as in an albino. When the error involves a vital function, abnormal products of altered metabolism may accumulate and exert toxic action, causing progressively irreversible and sometimes fatal damage, even at a very early age.

Phenylketonuria, for example, may be apparent in the first hours of life. Caused by the lack of a single essential enzyme, it can lead to mental retardation. Fortunately, a simple test has been devised to detect the condition, and, if begun early enough, diet therapy alone may prevent brain damage and enable the infant to develop normally.



Metabolic studies by NIAMD are aided by sophisticated instruments and volunteer subjects in establishing data on normal and abnormal metabolic states.

The exploration of space draws information from baseline data obtained through Institute research in metabolism.

Another approach to alterations of metabolism looks directly at patterns of chromosomes, the physical carriers of genetic information that may establish metabolic alterations. Only since 1956 has it been possible to obtain completely analyzable pictures of human chromosomes. The set shown is from a female (XX chromosomes).

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Woman is examined by an Institute investigator during epidemiological studies of arthritis, diabetes, and diseases of the gastrointestinal tract among Indians of the Southwestern United States.

Pima Indian girl on the Gila River Indian Reservation in Arizona drinks a sugary beverage prior to a blood-sugar determination as she takes part in an NIAMD survey of diabetes.

DIABETES

Of all the metabolic diseases, diabetes, which affects millions of people, is probably the best known. But it is not the best understood. In fact, the more we study diabetes, the more complexities and enigmas we see, the more we review and revise our theories concerning its origin and nature.

The high level of sugar in the blood and urine of diabetics is due to the body's inability to metabolize carbohydrates efficiently. Normally, carbohydrate metabolism is regulated by insulin, a hormone secreted by the pancreas. In the diabetic, there is an impairment of insulin activity. Either the body does not produce sufficient quantities of this substance, or the action of available insulin is somehow blocked.

In juvenile diabetes, the severe form of the disorder, evidence of the disease is frequently apparent in childhood or adolescence, as it may progress rapidly with serious complications involving blood-vessel damage in many parts of the body. Some cases result in blindness. Although the majority of patients with juvenile diabetes can be maintained for considerable periods with insulin therapy, life expectancy may be greatly shortened.

Maturity-onset diabetes, the other, much more prevalent form of the disease, usually has its clinical start after the age of forty and is generally less severe than that seen in young persons, not progressing so rapidly and so often to serious complications. Most of these patients do not require insulin and can maintain relatively normal blood-sugar levels by controlling their weight, adhering to a special diet, and using oral anti-diabetic drugs. While there is no permanent cure for diabetes, many patients, through dietary measures alone, can live long and active lives.

Clinical evidence showing that maturity-onset diabetics frequently have an ample supply of insulin—sometimes, even, a surplus—strengthens the concept that insulin action in these cases is somehow blocked—either destroyed or inactivated by antagonistic agents. Other research has shown that circulating insulin is, itself, a complex substance that must be examined more closely.

Another significant finding of NIAMD-supported studies—again in variance with conventional thinking—indicates that diabetes may be primarily a disease of the vascular system and not simply a disorder of carbohydrate metabolism.

These important findings now afford investigators new channels for research efforts. Continued advances depend upon further knowledge of the natural history of diabetes and its complications; of genetic factors; of how insulin is made in the pancreas, how it is transported, how it does its work, and how and by what agents it is destroyed, neutralized or inactivated in the performance of its vital tasks. Progress in these areas, now under intensive scrutiny, will contribute substantially toward the elimination or amelioration of diabetes and its consequences.

Surveys on the actual prevalence of diabetes also give clues to its causes. For several years, NIAMD scientists have been conducting field studies of the Pima Indians of Arizona, a population group that was found to have the highest rate of diabetes ever recorded in a circumscribed, apparently normal population group, a rate 10 to 15 times that of the U.S. population as a whole. This finding represents

a unique opportunity to explore the precipitating factors in diabetes, the progress of the disease and its complications, the role of diet and other environmental factors, and the effects of various therapeutic measures.

The diabetes study came as a by-product of one of the largest population surveys of rheumatoid arthritis ever attempted in the United States. This survey revealed new facts about arthritis, discrediting long-held theories that the disorder was inherited and was more severe in cold, damp climates.

More intensive studies of diabetes and arthritis among the Pimas, as well as new studies of gallbladder disease, are being conducted by NIAMD research teams. If the new studies are as fruitful as research already completed, and there is good reason to believe they will be, all Americans, as well as the Pima Indians, face a healthier future.

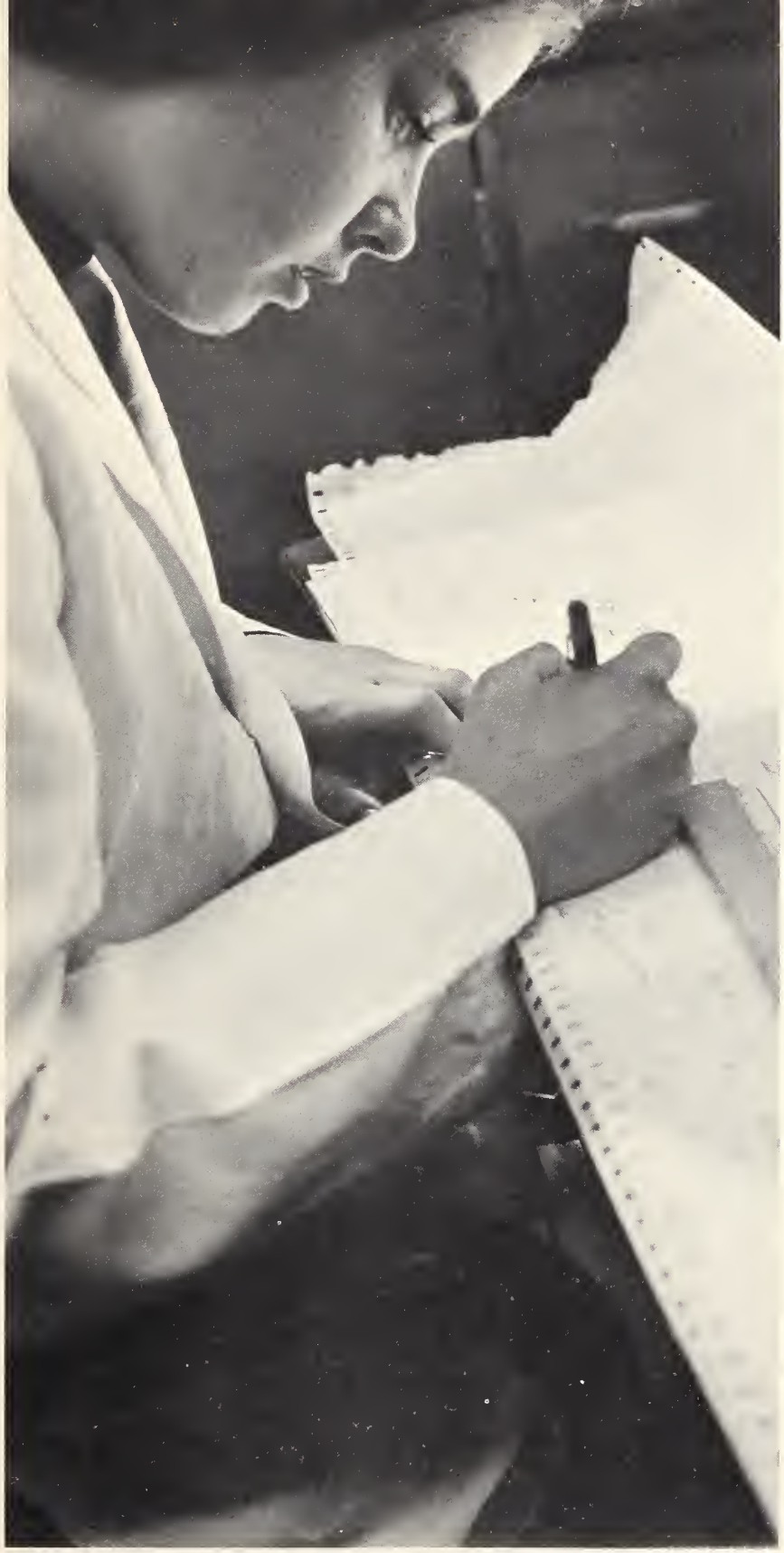
CYSTIC FIBROSIS

Cystic fibrosis is a generalized inherited disease of children and young adults caused by an unknown inborn error of metabolism that results in abnormal secretions of the exocrine ("outward-secreting") glands. In cystic fibrosis, the mucus glands of the intestines, liver and pancreas produce a thick, tenacious mucus which obstructs the intestines, pancreas and lungs, causing serious respiratory diseases and malnutrition. Simultaneously, a defect in sweat production results in excessive loss of salt.

As the disease continues, the usual story has been a steady deterioration in health and early death in childhood or in the teens. Currently, however, the outlook for individual patients is being improved by early recognition and by symptomatic treatment with antibiotics, pancreatic extracts, salt tablets and adherence to a regimen to maintain adequate lung function.

NIAMD scientists and grantees have developed reliable diagnostic tests based on the salt content of sweat, fingernails and hair, and have recently detected new factors in blood and saliva which affect the chemical content of saliva and action of bronchial cilia. Current research, employing sophisticated new tools also includes studies involving the normal sweating mechanism and its product under various conditions. Future plans call for extension of these studies to attempt to define the basic aberration in the chemical composition of sweat in cystic fibrosis, and also for exploitation of the new leads afforded by the finding of new humoral factors.

Paradoxically, as treatment of cystic fibrosis improves, more patients will survive to reach reproductive age and there may well be a proliferation of the gene in the population. If a method of correcting the basic genetic defect of the disorder is not discovered, an ever-increasing number of persons may find themselves heir to the disease. This factor, alone, makes unceasing, intensive and fruitful research on cystic fibrosis a prime obligation.



A laboratory technician records data from cystic fibrosis studies on graph paper. The basic defect underlying this disease, serious hereditary disorder of children, is as yet unknown.

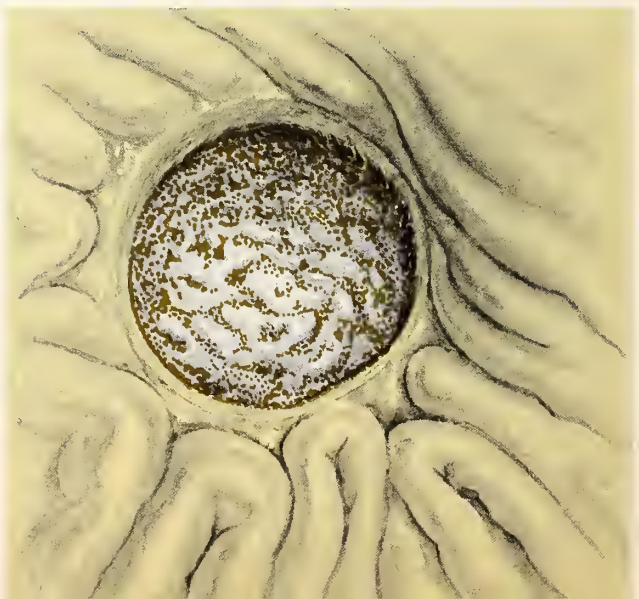
GASTROENTEROLOGY

Peptic ulcer, regional ileitis, ulcerative colitis, liver and gallbladder disease—these are just a few of the multifarious disorders of the digestive tract that come under the medical specialty "gastroenterology" and rank among the most common illnesses in the United States. While we are well acquainted with their symptoms—peptic ulcer strikes more than 10 percent of American adults at some time in their lives—we, unfortunately, are not on such familiar terms with their causes and modes of action. In order to correct this situation, in recent years NIAMD has greatly expanded its efforts in gastroenterological research, and most of the new impetus in this important field is due to the active support extended by the Institute in the development of new ideas and techniques.

Significant research findings are systematically providing promising leads and approaches in the search for improved diagnosis and treatment of gastrointestinal disorders which afflict persons of all ages but mostly young and middle-aged groups at the peak of their productivity. In an important recent breakthrough by NIAMD grantees in England, the chemical nature and structure of gastrin, the hormone which stimulates secretion of gastric juices, was elucidated and the hormone was subsequently synthesized. This synthesis of gastrin is particularly important in research in peptic ulcer, a condition in which there is an excessive production of gastric digestive juices. Investigators now have a potent secretory stimulant for assessing gastric function and determining if and how this varies in normal and peptic ulcer patients.

While substantial progress has been made, the problems of gastroenterology still loom as a formidable challenge. The causes of many of these disorders seem to lie in highly complex and varied interactions.

NIAMD plans increased efforts for training of investigators for gastroenterological research, expansion of studies aimed at overcoming temporary acute liver failure and at effective liver transplantation, and increased research on peptic ulcer, gallbladder disease, ulcerative colitis and other disorders of the gastrointestinal tract.



A peptic ulcer is a noncancerous, crater-like sore (called an erosion) in the wall of the stomach or intestine.

Technician adjusts instrument which will aid in precise positioning of a protein crystal for a study of its structure through X-ray diffraction.

Exceedingly potent venom from frogs such as Dendrobates pumilio, *originally collected on Bastimentos Island, Panama, is studied for information on steroid hormones. One type of venom has been found to be chemically related to these hormones.*

ENDOCRINOLOGY

Endocrinology concerns itself with the endocrine glands (internally-secreting, hormone-producing glands like the pituitary, thyroid and adrenal glands or the ovary and testis), and with the effect of hormones on the metabolism and physiology of man. A wide spectrum of problems is involved, as the endocrine system, in close cooperation with the nervous system, controls almost all the metabolic, growth and reproductive functions of man.

Endocrinology is one of the cornerstones of modern clinical and biomedical research. NIAMD supports the bulk of endocrinological research at NIH, and bears responsibility for the classic endocrine disorders, such as hypo- and hyperthyroidism, hypo- and hyperpituitarism, and adrenal disorders.

In recent years, great strides have been made in our knowledge of the hormones and in the laboratory synthesis of specific hormones. The chemical syntheses of pituitary adrenocorticotropin (ACTH) and of insulin constitute milestones in endocrinological and chemical research. The development under NIAMD support of new endocrine methods for birth control and for treatment of sterility has received wide attention. To a large extent, an ability to diagnose and treat most classical endocrine syndromes has been achieved.

Yet, lack of fundamental knowledge of the precise mechanisms by which hormones influence metabolism, and of how hormones react with each other, still hinders greater progress.

OSTEOPOROSIS

Osteoporosis is a disorder with mixed metabolic and endocrine background. It afflicts a large percentage of women over 50 years of age, and many older men. Causing a gradual decrease in both the amount and strength of bone tissue, osteoporosis is often the real cause of the numerous broken hips which hospitalize so many older people and, in many cases, start their physical decline. This disease is one of the major causes of physical disability in old age, especially in women.

NIAMD investigators have found that diets high in calcium may offset further bone-thinning in many osteoporotic patients. Hormonal replacement in women beginning shortly before or at the menopause is another important preventive measure. But, as yet, no overall effective corrective treatment of the disorder has been devised.

With increased awareness of the prevalence and significance of osteoporosis, studies on the involvement of nutritional, hormonal and genetic factors in the disease are being intensified and broadened. Plans have been made for a world-wide collaborative study on the epidemiology of osteoporosis.

HUMAN GROWTH HORMONE (HGH)

The relationship between pituitary hypofunction and dwarfism has long been known. A specific hormone elaborated by the pituitary gland, the growth hormone, regulates the rate of growth of the individual. A deficiency in the secretion of human growth hormone (HGH) results in growth impairment, and, if severe enough, in hypopituitary dwarfism. Repeated unsuccessful attempts have been made to treat this condition with *animal* pituitary extracts. Recently,

it has been shown that hypopituitary children can grow to a near normal height when treated with purified growth hormone extracted from human pituitary glands taken from cadavers. Unfortunately, there is a severe shortage of human growth hormone (HGH). Thousands of children need treatment but it is difficult to obtain enough pituitary glands. (The amount of HGH derived from one pituitary gland will provide treatment for a dwarf for only one or two days.)

In an effort ultimately to relieve this situation and to provide increased quantities of HGH for research, NIAMD has created by contract the National Pituitary Agency at the University of Maryland to provide for the collection of human pituitary glands, for the extraction of purified HGH and other pituitary hormone fractions therefrom, and for the distribution of HGH for selected laboratory and clinical research.

In addition, Institute research grants are supporting investigations aimed at the possibility of modifying animal growth hormone to make it effective in humans, and at methods for laboratory synthesis of the hormone. Until one of these goals is achieved, the sole source of HGH is the human pituitary gland which is obtainable only at autopsy.

NUTRITION

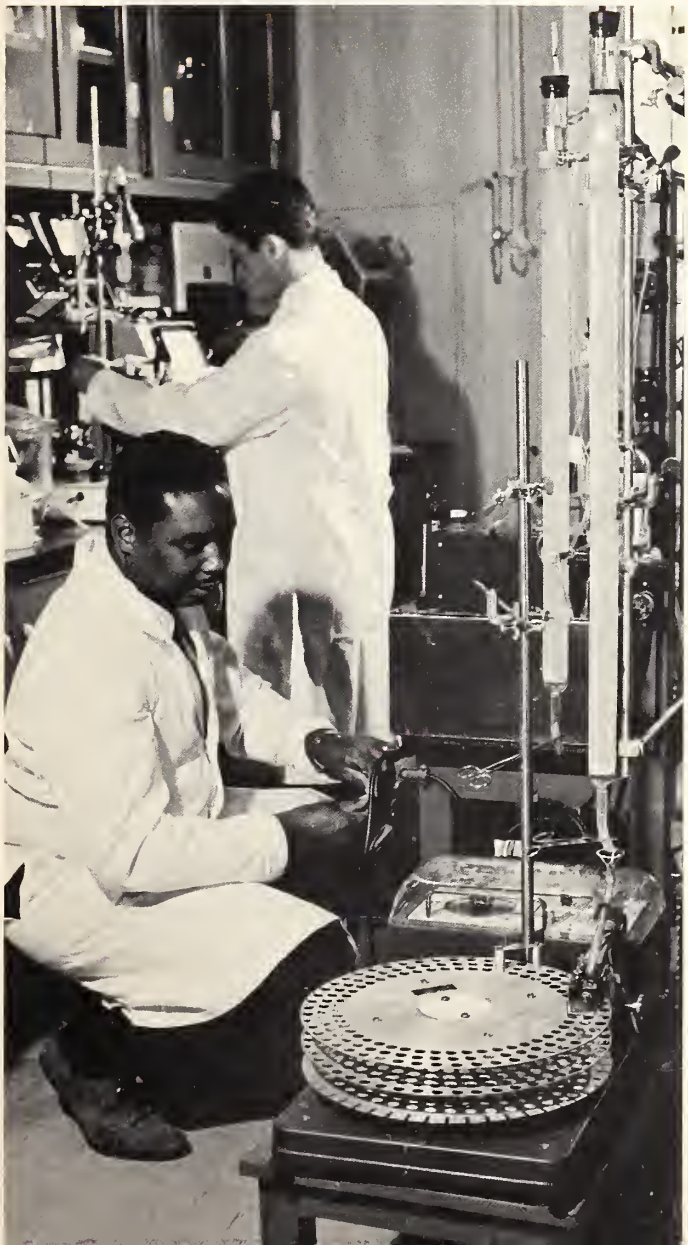
With the passing of the early era of vitamin and mineral deficiency diseases, such as scurvy, pellagra, and rickets, the most important nutritional problem in the United States today is no longer underconsumption of nutrients but overconsumption of calories. About 20 percent of all adults are overweight to a degree that impairs health and longevity. Diet and obesity appear to be significant factors in the causation, prevention and treatment of many diseases, including atherosclerosis, diabetes, hypertension, and gallbladder disease, to name a few.

Because of the public health importance of obesity, a large number of studies on the problem are supported by NIAMD. These studies deal with the effect of dietary variations (such as fasting and the spacing of meals); with body composition and nutrient metabolism; and with the relationship of diet to lifespan and chronic degenerative diseases. Other nutrition research involves deficiency diseases (such as kwashiorkor, caused by severe protein deficiency) which are still prevalent in many underdeveloped countries and study of the biochemical, metabolic and physiologic roles played by specific nutrients.

Future programs call for an intensification of studies on many aspects of obesity, including appetite regulation and food intake, and expanded applied research efforts aimed at the provision of improved nutrition to vulnerable population groups in underdeveloped countries and, where the need exists, in the United States.

Adding a new dimension and challenging new approaches to medical and biological research in recent years has been the development of germfree animals and germfree research techniques, in which NIAMD scientists and grantees have been pioneers. Observations of animals reared in an experimental world without bacteria—animals that are born free of germs, eat germfree food, drink germfree water, breathe germfree air and produce new generations of germfree offspring—have made valuable contributions to knowledge of man's intestinal microflora and its effect on his vitamin supply and metabolism.

In India, the NIAMD is engaged in nutrition research, while helping that Nation develop more adequate foods for its undernourished populations. Indian housewives demand wheat familiar in appearance and taste to grind at the village flour mill. Researchers may coat the grain with lysine, a component of good protein.



A scientist weighs a germfree rat in a nutrition experiment. The animal is housed with necessary supplies and equipment in a germfree tank.

Investigators prepare for experiments employing column chromatography, a means of separating different fractions of a substance.

RENAL DISEASES AND THE ARTIFICIAL KIDNEY

Kidney diseases of one kind or another kill tens of thousands of Americans annually. Until recently, there was little hope for the victim of uremia, the progressive toxic condition caused by kidney failure and the resulting accumulation of waste products in the blood.

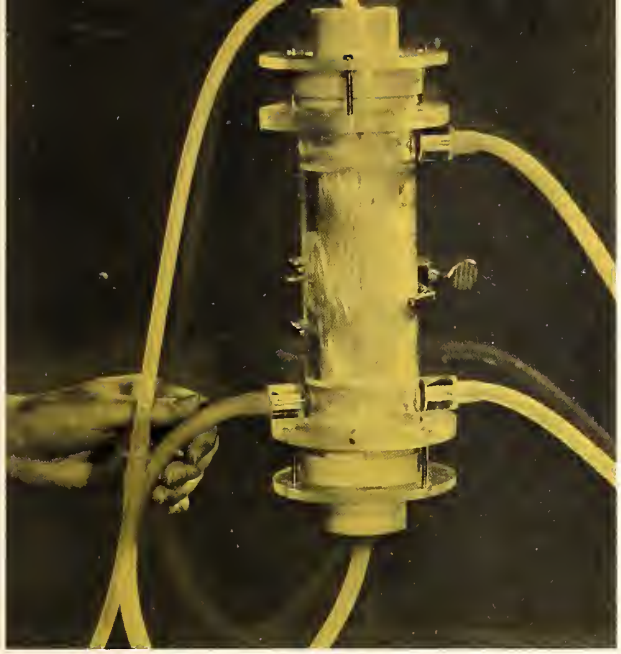
Today, a small percentage of patients with chronic kidney failure is being kept alive and productive by repeated use of artificial kidney machines, mechanical devices that can be used to cleanse the blood when the natural kidneys cease to function. Until the time when transplantation of healthy kidneys from live or dead donors becomes a routinely successful procedure—when the tendency of the body to reject the transplanted tissue is medically overcome—repeated hemodialysis, blood purification through the use of an artificial kidney, is the best hope of survival for patients with chronic, progressive renal failure.

Although artificial kidneys have been known for some time and have been used in emergency cases of poisoning or acute (temporary) kidney failure, only in recent years has routine use of these machines on a twice- or thrice-weekly schedule become feasible, as the result of a device which makes it possible to connect a patient repeatedly to artificial kidneys without surgical procedures. Development by NIAMD grantees of permanently implanted, connected plastic tubes in an artery and a vein of the forearm or leg of the patient started a new era of life-saving treatment for patients with end-stage kidney failure.

Patients maintained with the aid of artificial kidneys, however, still display a number of undesirable symptoms. Also, the cost of currently available techniques is too high, both in terms of money and qualified manpower, to permit permanent widespread patient treatment.

Hemodialysis techniques and equipment require considerable improvement, which must come about through research and development. Moreover, fundamental research on uremia must proceed simultaneously because authorities agree that optimal improvements in hemodialysis depend substantially on additional knowledge of the nature of uremia.

NIAMD has instituted a special, contract-funded Artificial Kidney Program aimed at developing simpler, safer, more effective and less expensive artificial kidney treatment for patients with chronic kidney failure. In addition, the Institute has embarked on an intensive program to achieve a better understanding of kidney diseases and chronic kidney failure. From improved methods of diagnosis of kidney disease to improved techniques of kidney transplantation, the Institute, through a sizeable program of extramural grants is supporting a wide variety of approaches to ensure a comprehensive attack on the whole problem of kidney disease and urologic disorders.



New compact artificial kidney developed under an Institute contract has proved highly successful in human trials.

Patient using artificial kidney.

BLOOD AND SKIN DISORDERS

NIAMD-supported research has contributed much to current knowledge of anemias and other blood disorders. Diagnostic techniques, the key to successful treatment, have become highly developed. Substantial advances have recently been made in the physical chemistry of blood-clotting mechanisms and in the understanding of "bleeding" disorders such as hemophilia.

In recent years, much skin disease research has been focused upon psoriasis, a common condition in which faulty epidermal metabolism results in disfiguring lesions. Studies financed by NIAMD have indicated that this is an inherited disease. At present, Institute grantees are engaged in identifying certain cellular malfunctions in the skin with specific biochemical disturbances in an attempt to gain a better understanding of the causes and development of the various skin disorders. Side by side with research grant support, the Institute maintains a sizeable program of graduate research training in the fields of hematology and dermatology.

SPECIAL ACTIVITIES

SCIENTIFIC COMMUNICATIONS

"Current awareness" periodicals, containing bibliographic references and abstracts of the world's current biomedical literature of interest and significance to investigators and practitioners in fields represented by NIAMD are published by the Institute. These publications furnish much-needed central sources of specialized up-to-date information provided at present by no other publication, and make available to American investigators a wealth of pertinent scientific literature published in foreign languages abroad. Current publications are: *Arthritis and Rheumatic Diseases Abstracts, Diabetes Literature Index, Gastroenterology Abstracts and Citations,* and *Endocrinology Index.*

As the recipient of a multitude of scientific research and development reports resulting from its Artificial Kidney Program, the Institute plans to serve as a reference and communications center for research information on artificial kidneys and dialysis for the investigators, practitioners and manufacturers involved in dialysis and chronic uremia research, both in the United States and abroad. Regular publications include the quarterly *Artificial Kidney Bibliography,* a comprehensive report of research and development contract findings, technical monographs, and printed proceedings of annual working conferences relevant to clinical aspects of chronic uremia.

MATHEMATICAL RESEARCH

The growing importance of research on the mathematical and theoretical aspects of biological problems is reflected in NIAMD's Mathematical Research Branch. Staffed by scientists who have had primary training and experience in some biological area before turning to mathematical research, the Branch initiates basic research projects that often develop into close collaborative efforts with biomedical scientists.

Mathematical research is developing useful mathematical and computational methodologies—theoretical models—to test hypotheses about biological systems. The advent of electronic computers, has raised mathematical and theoretical research to new heights of sophistication and researchers in this field are making great strides toward solutions to specific biomedical problems while continually improving methodology and treatment.

Data is received on this machine over telephone lines from a central computer serving several different groups of investigators.

A GLIMPSE INTO THE FUTURE

Although recent years have been among the most productive in terms of advances in biology and medicine, the future promises even more important and exciting developments in man's battle against disease. Extensive growth in the areas of biophysics and biomathematics, resulting in increased precision of measurement and thought, is anticipated. New developments in instrumentation and collaborative effort by well-balanced teams of investigators, representing a variety of disciplines never before concentrated in coordinated efforts, offer approaches to previously unassailable, age-old problems.

The Institute's research and training programs, both intramural and extramural, are expected to continue their steady expansion in size and scope. Good research, of course, requires not only financial support but the manpower to carry it out. One of the most fruitful programs of the Institute has been its support of the research training of young biomedical scientists in fields within its purview. These training grants and fellowships to individuals with promising talent have been designed to alleviate the constant threat of a serious shortage of scientific manpower. Without such manpower, the high standards of excellence now expected of those engaged in modern day biomedical research will be diluted, and the urgent needs of the public in respect to chronic illness, no matter how generous budgetary allowances may be, will not be met.

In the period ahead, increased knowledge gained by stepped-up research will necessarily alter many phases of clinical medicine. As the understanding of causes is elucidated, the classification of disease will become more meaningful. Once the metabolic, physiologic or genetic defect causing a disease and the process underlying the defect are thoroughly understood, therapy will move from the empirical or experimental, where it largely resides today, to the rational and purely scientific.

Institute scientists confidently expect that the future design of therapy will rest securely upon a solid foundation of knowledge, that the treatment of tomorrow will be custom-made to correct a clearly defined biologic defect.

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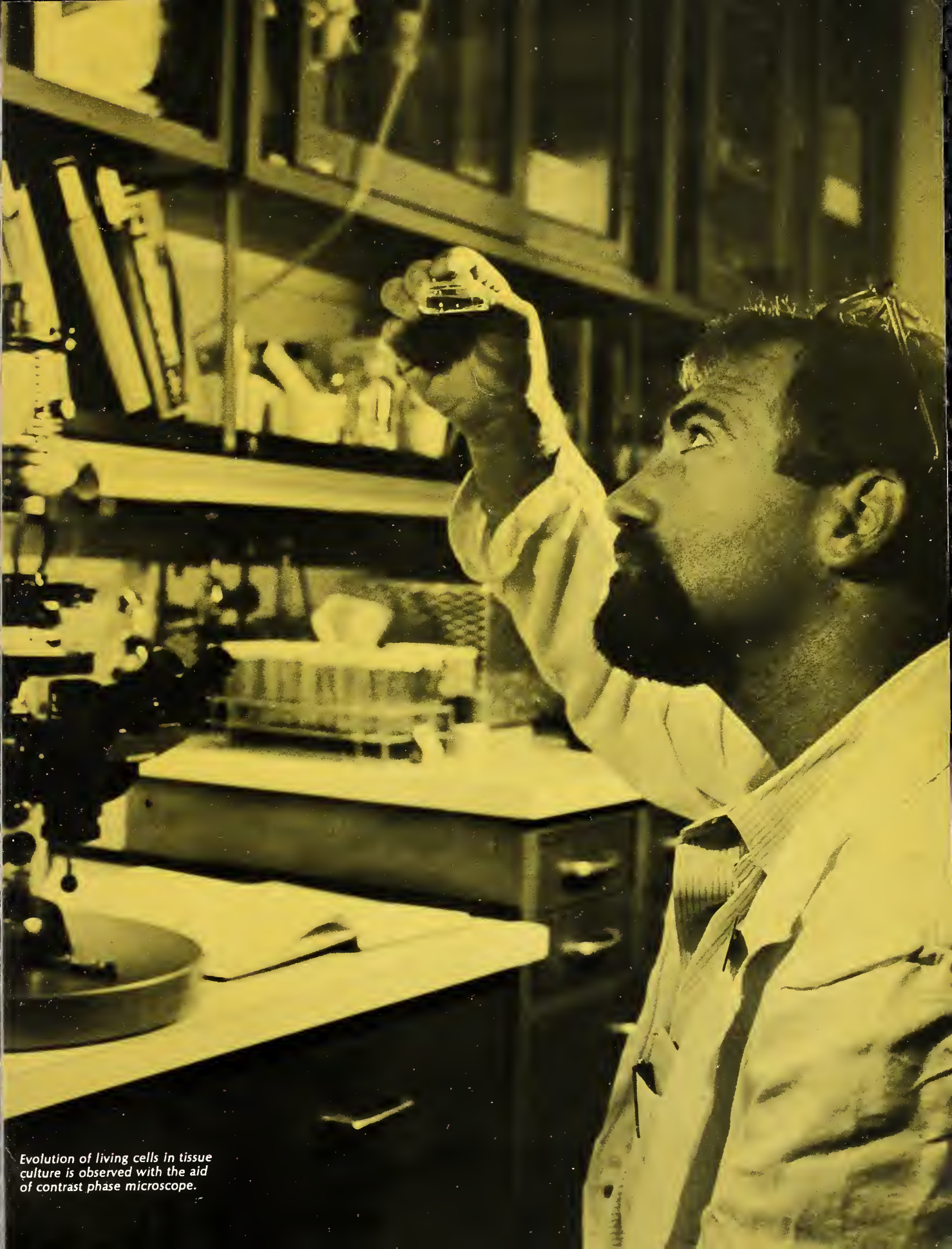

Evolution of living cells in tissue culture is observed with the aid of contrast phase microscope.

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